REMARKS

Status of the Claims.

Claims 1-53 are pending with entry of this amendment, with claims 32-37 and 39-52 being cancelled and withdrawn from current consideration. Cancellation of these claims is without prejudice, without intent to abandon any originally-claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants expressly reserve the right to file one or more continuing applications containing these cancelled claims.

In the current Office Action, claim 4 was objected to for containing non-elected subject matter. Claims 18 and 38 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification so as to enable one skilled in the art to make and/or use the invention, while claim 18 was also rejected as requiring undue experimentation to make and use the claimed invention. Additionally, claims 3 and 4 were rejected under 35 U.S.C. §112, first paragraph as allegedly containing subject matter not described so as to convey to one skilled in the art that Applicants possessed the claimed invention at the time of filing. Claims 2-5, 7, 14, and 26-28 were rejected under 35 U.S.C. §112, second paragraph as purportedly being indefinite. Claims 1-3, 5, 9-11 and 31 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Ivanov et al. and claim 30 was rejected under 35 U.S.C. §102(b) as allegedly anticipated by Martinez-Salas et al. Finally, claims 6-8, 12-17, and 19-29 were rejected under 35 U.S.C. §103(a) as allegedly obvious in regard to Santa Cruz et al. in view of Ivanov.

Claims 1-4, 8, 14-15, 19, 23, 27-28, and 30 are amended herein and claims 6, 31, 32-37 and 39-52 are cancelled. New claims 53-56 are added herein. These amendments introduce no new matter and support for such is replete throughout the specification and claims as filed.

In regard to any rejection or objection remaining after entry of the current amendments, Applicants respectfully traverse each of such objections and rejections for the reasons explained below.

Information Disclosure Statement.

Applicants submit herewith a supplemental Information Disclosure Statement and Form 1449 to be made of record in the present matter.

Election/Restriction.

Pursuant to the previous restriction requirement, Applicants cancel claims 32-37 and 39-52 with entry of this amendment. Please note, however, that Applicants reserve the right to file subsequent applications claiming the canceled subject matter and that the claim cancellations should not be construed as abandonment or agreement with any adverse position in the Office Action.

Additionally, Applicants note that the election of species made in the Response to Restriction mailed December 2, 2002 should not be construed as a restriction. Applicants' election of one sequence is a species election, not a restriction. However, in order to further prosecution, Applicants herein amend the claims (*see*, below) to recite only SEQ ID NO:1. Again, please note that Applicants reserve the right to file subsequent applications claiming the non-elected sequences and that amendments herein should not be construed as abandonment or agreement with the Examiner's position in the Office Action or Restriction Requirement.

Objections to the Claims.

Claim 4 was objected to as containing non-elected subject matter (i.e., recitation of species other than that elected). Claim 4 is amended herein to not currently include sequences other than SEQ ID NO:1. Thus, Applicants respectfully request that the objection to claim 4 be withdrawn.

35 U.S.C. §112, Second Paragraph.

Claims 2-5, 7, 14 and 26-28 were rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite. More specifically, claims 2-5 and 7 were alleged to be indefinite due to their use of "promoter" and their recitation of "(1)", "(2)", etc. Claim 14 was purported to be indefinite for insufficient antecedent basis for recitation of "reporter gene," while claims 26-28 were alleged to be indefinite because of their use of the word "derived." Applicants kindly note the Examiner's observations and herein amend claims 2, 3,4, 14, and 26 and add new claim 53. Additionally, Applicants also amend claim 26 to correct an additional antecedent basis issue. These amendments clarify the issues regarding various recitations and further define the claimed invention. No new material is added by these amendments and Applicants believe the amended claims to be definite within the meaning of 35 U.S.C. §112 and therefore respectfully request that the rejections be withdrawn.

35 U.S.C. §112, First Paragraph.

Claims 3, 4, 18 and 38 were rejected under 35 U.S.C. §112, first paragraph. Claims 3 and 4 were rejected as allegedly containing subject matter not described in the specification in a way as to reasonably convey to one skilled in the art that the Applicants possessed the claimed invention at the time of filing. Claims 18 and 38 were rejected as allegedly containing subject matter which was not described in the specification so as to enable one skilled in the art to make and/or use the invention while claim 18 was also rejected as allegedly requiring undue experimentation to make/use the claimed invention. Applicants respectfully traverse.

Claims 3 and 4

In regard to claims 3 and 4, the Office Action alleges that the specification only discloses IRES from Tobamovirus. The Office Action alleges that the specification is inadequate because it "does not disclose any other naturally occurring IRES that can direct translation *in vitro*;" the size and exact sequence needed to function as an IRES is not described; and a number of representative species are not described by their complete structure (or identifying characteristics), etc. The Action implies that a description of a representative number of species by their complete structure or other relevant identifying characteristics is needed. Applicants respectfully traverse.

As the Examiner helpfully pointed out, possession may be shown by describing the invention "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." Office Action at page 5, quoting Lockwood v. American Airlines Inc. 107 F.3d 1565. Such description must convey to one skilled in the art that Applicants were in possession of the invention at the time of filing. *See*, e.g., Vas Cath v. Mahurkar 935 F.2d 1555. Additionally, M.P.E.P §2163(I)(A) indicates that lack of possession would exist where "the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art" or where "the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed."

By applying such tests as outlined in the M.P.E.P., Lockwood and Vas Cath, it can be seen that the specification does indeed describe the invention so as to convey to those skilled in the art that Applicants were in possession of the invention at the time of filing. The specification is replete with description of IRES. Additionally, structures/functions/etc. of IRES were known to those of

ordinary skill in the art at the time of filing. Therefore, additional listings of complete structures or sequences of other IRES, etc. is unnecessary.

The term IRES as described in the specification, and used in claim 3 and 4 comprises "a nucleic acid sequence which involv[es] direct recruitment of ribosomes to internal tracts within mRNAs. [...] Specific sequences, termed IRES direct the translation of mRNAs with different functions, under different physiological conditions". *See*, page 6, lines 22-26 and page 6, line 27 through page 7, line 5. Additionally, the specification emphasizes that,

> IRES can be an IRES from any organism as long as that IRES is able to function as an IRES within a host. The IRES can be from an animal (such as a mammal), plant, or a virus. The IRES nucleotide sequence can be a viral IRES. In a more preferred embodiment the IRES nucleotide sequence is an IRES of a plant virus. In a more preferred embodiment the IRES nucleotide sequence is an IRES of a plant RNA virus. In an even more preferred embodiment the IRES nucleotide sequence is an IRES of a tobamovirus. In an even further preferred embodiment the IRES nucleotide sequence is an IRES of a crucifer-infecting tobamovirus. *See*, page 8, line 25 through page 9, line7.

Additionally, numerous references concerning and describing IRES are listed in the application on pages 23 through 26. Thus, those skilled in the art will recognize that many different species have natural IRES and have been studied sufficiently enough to be known by those of skill in the art and used in the current invention. Those skilled in the art will know that IRES sequences occur naturally in numerous organisms and had been known for over a decade at the time of filing. Many of such IRES were also fully sequenced. Indeed the USPTO database indicates numerous issued U.S. patents and published U.S. patent applications mentioning "internal ribosome entry sites." Furthermore, a brief search of public databases such as Medline, shows numerous journal articles containing "internal ribosome entry sites" published before the filing date of the current application (e.g., roughly at least 375 journal articles referencing "internal ribosome entry sites" published before filing of the current application). Also many IRES outside the Tobamovirus family are known. References cited in the current Office Action, e.g., Martinez-Salas et al., include helpful examples. Therefore, one skilled in the art will understand that the description and examples in the

current application are more than enough to convey that Applicants were in possession of the claimed invention at the time of filing.

In terms of IRES fragments, as can be appreciated from the specification, different IRES sequences comprise different lengths and the exact boundaries of each are variable. For example, the IRES sequences described in the specification as SEQ ID NO: 1-7 contain sequences with six different lengths. Thus, any shorter sequence, including some of those exemplified, can be considered as being a fragment. However, fragments of IRES sequences in the claims in question are limited/defined in the claims as being able to direct translation of an ORF. Since the functional abilities/requirements of the IRES and the IRES fragment, as defined in the claims, are overlapping, the specification provides a written description of both as required by 35 U.S.C. §112, first paragraph.

Applicants submit that the description in the specification is more than adequate for one of ordinary skill in the art to understand and choose from among the many known IRES sequences at the time of filing. Furthermore, since the IRES fragment lengths are delineated by the requirement of translation of an ORF, Applicants submit that those of skill in the art will easily grasp the parameters of such fragments. More intricate information on exact sequences, structures, and/or characteristics is, thus, not necessary. Accordingly, the description in the specification is sufficient to support "IRES" in its fullest scope envisioned. Applicants respectfully request that the rejections be withdrawn.

Claim 18

In regard to claim 18, the current Office Action alleges that "[I]n view of the teaching of the specification and art, one skilled in the art would have to engage in undue experimentation to make and use such construct as claimed." In other words, the Office Action purports that because the specification does not disclose, and the prior art does not teach, a potato virus X viral vector comprising a viral genome, an IRES and a virus coat protein gene which gives rise to single cell infection sites, then undue experimentation would be required to arrive at such a construct. Applicants respectfully traverse.

For analysis of "undue experimentation," the M.P.E.P. in §2164.02 (quoting In re Wands at 1404) states, that

> [t]he test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the

specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

Based upon such criteria, Applicants respectfully hold that the claims as given are indeed enabled by the specification as filed and that no undue experimentation is required.

More specifically, numerous examples of such constructs which give rise to single cell infection sites are given in the specification. For example, single cell infection sites can arise because CP, which is needed for cell to cell movement, is not translated due to loop structures 3' to the IRES. Thus, page 14, lines 16-22 of the specification describes exemplary IRESH vectors having viral genome, IRES, and a viral coat protein. Further description and characterization of such constructs can be seen, e.g., on page 5, lines 5 through 7 of the specification which describes Figure 2B. As described "Figure 2B depicts confocal images of inoculated *N. benthamiana* leaf tissue, 5 days post infection, **showing single cell infections** with TXS.GFP-IREScpH-CP." Emphasis added. Additionally, page 16, line 29 through page 17, line 5, shows similar constructs and explains that even though coat protein nucleic acids are present, such sequences are not translated and, thus, no coat protein is produced. Additionally, page 18, lines 13-15 and page 18, Table 1 also describe constructs from which no CP was translated and, thus, no cell to cell movement occurred. Also, page 22, lines 2-4 (directly after the sentence cited by the Office Action) reemphasizes the same point.

Because of such broad support throughout the specification, Applicants submit that the specific examples of single cell infection sites give more than reasonable guidance for any experimentation that may be needed. Thus, Applicants respectfully request withdrawal of the rejection.

Claims 18 and 38

Finally, in regard to 35 U.S.C. §112, first paragraph, claims 18 and 38 were rejected as containing subject matter not described in the specification so as to enable one skilled in the art to make and/or use the invention. In particular, the Office Action alleges that the information given by Applicants on page 12 of the specification does not meet the rule regarding deposit of biological materials. Applicants respectfully traverse.

Applicants are somewhat confused by the Office Action's list of requirements regarding deposit of biological material. The requirements for description in a specification of a biological deposit are listed in M.P.E.P. §2411 which interprets 37 CFR 1.809. The requirements include that

> [f]or each deposit made pursuant to these regulations, the specification shall contain; (1) The accession number for the deposit; (2)The date of the deposit; (3) A description of the deposited biological material sufficient to specifically identify it and to permit examination; and (4) The name and address of the depository.

Applicants respectfully point out that page 12 clearly lists the accession numbers for each deposit, the date of deposit, a description of each deposit, and the name of the depository (ATCC). To help expedite prosecution, Applicants herein attach a copy of the deposit receipt from the ATCC verifying deposit of the biological material.

35 U.S.C. §102.

In the current Action, claims 1-3, 5, 9-11 and 31 were rejected under 35 USC 102(b) as being anticipated by Ivanov et al. Applicants amend in part and traverse in part.

Applicants respectfully point out that Ivanov cannot anticipate the current claims because Ivanov does not include all the limitations of the current claims. In order for a reference to anticipate a claim M.P.E.P. § 2131 requires that all elements of the claim in question be present in the cited reference.

> A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.
> M.P.E.P. §2131 citing *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2s 628, 631 (Fed. Cir. 1987).

Applicants respectfully point out that Ivanov does not meet this requirement.

While Applicants believe that the unamended claims are distinct from Ivanov, claim 1 (and, thus, its dependents) is amended herein to further emphasize the differences between the current invention and Ivanov. It should be noted that claims 6 and 31 are cancelled herein due to redundancy arising from the current amendments.

Even though the Office Action describes a plasmid construct from Ivanov as allegedly teaching the all of the limitations of the current claims, such plasmid is not equivalent to the recombinant plant viral vectors of the instant claims. Specifically, the claims of the present invention are drawn to a recombinant plant viral vector, while Ivanov is drawn to various non-

infectious plasmids. As is clear from the specification, such plant viral vectors (with IRES, etc.) are optionally used to infect plants *in vivo* and, in particular cases, to systemically spread throughout a plant. The present invention comprises plant viral vectors comprising, e.g., "modified virus capable of expressing a desired protein or trait in a host." *See*, page 6, lines 4-5. This is as opposed to Ivanov which comprises plasmid constructs to be used *in vitro*, which might contain some viral genes in their sequence. The differences between the two approaches will clearly be appreciated.

While claim 1 is amended herein, Applicants point out that claims 9-11 already contain language concerning heterologous viral vectors, which, as outlined above, are distinct from the types of constructs used in Ivanov.

Thus, because the current claims, as opposed to Ivanov, comprise recombinant viral vectors which are capable of *in planta* use (as illustrated by the Examples in the specification, etc.), Ivanov does not teach every element of the current claims, and, thus, cannot anticipate the current claims. Applicants, therefore, respectfully request that the rejections be withdrawn.

Claim 30 was rejected under 35 USC 102(b) also, as being anticipated by Martinez-Salas et al. Claim 30 is amended herein to further emphasize distinctions between the current invention and the disclosure of Martinez-Salas. Thus, amended claim 30 teaches a plant viral vector. Martinez-Salas on the other hand is drawn to animal viruses (e.g., foot and mouth disease virus). Because of the differences between amended claim 30 and Martinez-Salas, Applicants respectfully request that the rejection be withdrawn.

35 U.S.C. §103(a).

Claims 6-8, 12-17, 19-29 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Santa Cruz et al. in view of Ivanov et al. The Office action alleges that it would have been obvious to one of ordinary skill in the art to combine the references to "construct a PVX based viral vector comprising GFP, IRES and CP gene" as well as to "construct a PVX based viral vector comprising GFP, IRES and CP gene with stem loop structure upstream or downstream." Applicants respectfully traverse.

Three requirements must be met for a prima facie case of obviousness from combined references. First, there must be a motivation to modify the reference(s) or combine the teachings to produce the claimed invention. M.P.E.P. §2143.01. Second, there must be a reasonable expectation of success. M.P.E.P. §2143.02. Third, the prior art reference(s) must teach all of the limitations of

the claims. M.P.E.P. §2143.03. Furthermore, the teaching or suggestion to combine, and the expectation of success, must both be found in the prior art and not based upon the disclosure of the Applicants. M.P.E.P. §2142. Applicants respectfully point out that these requirements have not been met for a prima facie showing of obviousness for any of the cited references or combinations thereof. Such lack of prima facie obviousness is true for both the unamended claims as well as for the amended claims herein.

In regard to Santa Cruz in view of Ivanov, Applicants respectfully point out that such combination fails to meet the criteria explained above. First, and quite importantly, even assuming, *arguendo*, that all of the elements of the amended claims exist in the cited references, there is no motivation or expectation of success to combine the references. As explained by the M.P.E.P., the motivation and expectation of success must be supplied by the cited references not by the current application. No such motivation or expectation exists in either Santa Cruz or Ivanov.

The Office Action suggests that motivation would exist because increased expression would occur. However, this is not enough to establish prima facie obviousness. As stated in the M.P.E.P., the "mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggest the desirability of the combination." M.P.E.P. §2143.01 quoting In re Mills 916 F.2d 680. Additionally, a "statement that modification of the prior art to meet the claimed invention would have been " 'well within the ordinary skill of the art' . . . is not sufficient to establish a prima facie case of obviousness without some object reason to combine the teachings of the references." M.P.E.P. §2143.01 quoting Ex parte Levengood 28 USPQ2d 1300. The Office Action points to no citation in either reference which would provide the needed motivation to combine. Thus, since the motivation to combine does not exist in either reference, a prima facie case of obviousness cannot exist and the rejection should be withdrawn.

Additionally, there is no expectation of success in combining the two cited references. As with motivation to combine, the expectation of success must be found in the prior art and not be based on the Applicants' disclosure. M.P.E.P.§2142. Again, the references cited do not show in themselves any expectation of success for combination. In fact, Ivanov and Santa Cruz are quite dissimilar in content and aim, so an expectation of success in combining them would not arise. For example, Ivanov is focused on an in vitro system while Santa Cruz is focused on an in vivo system. Furthermore, the two methods differ greatly in their translation strategies, namely, Ivanov uses IRES sequences having multiple translation events while Santa Cruz uses a single translation event with

cleavage of a fusion protein. Due to the disparities in the systems, there is no reasonable expectation that the addition of an IRES sequence to Santa Cruz's structures would give better results. Prior to actually testing such construct, it would be speculation to assume that an IRES in such a different construct (i.e., Santa Cruz) would induce superior results for coat protein expression. In addition, Santa Cruz states that they intended to generate both free and fused proteins, not just cleaved (i.e., separate) GFP and CP. *See*, Santa Cruz, p. 6287, col. 2, first sentence of 2nd paragraph of "Results and Discussion." Furthermore, based upon the disparities of the systems as outlined above, Ivanov and Santa Cruz do not present an expectation of success to suggest a combination of stem-loop structures upstream/downstream of the IRES in such a vector. Because the two references do not present an expectation of success, the rejection should be withdrawn.

Thus, since the references do not present, either singly or combined, all three required elements, a prima facie case of obviousness under §103(a) has not been met. Applicants therefore respectfully request that the rejections be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 337-7871.

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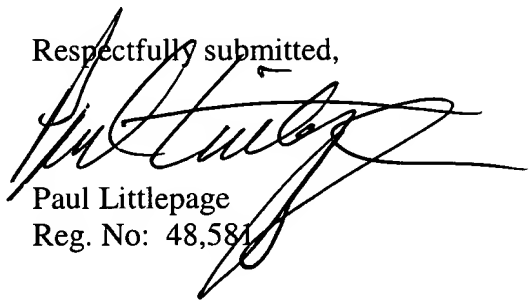
Respectfully submitted,



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